Preparing for bioterrorism

PEGGY LATHROP, RN, BSN, CIC, AND LINDA M. MANN, PhD, D(ABMM)

CME

CME, Part 1 of 3

Target audience: All physicians

Learning objectives:

1. Identify governmental initiatives to prepare for bioterrorism.
2. Describe characteristics of anthrax, botulism, plague, and smallpox and the precautions to be used when dealing with patients who have been exposed to these agents.
3. List several clinical situations in which the health care provider should have a high degree of suspicion for bioterrorism.
4. Know how to respond to 3 scenarios of bioterrorist attack: the hoax, the massive attack, and the small or covert attack.

Faculty credentials/disclosure:

Ms. Lathrop recently retired from the Department of Epidemiology at Baylor University Medical Center and participated in the bioterrorism task force of the Dallas-Fort Worth chapter of the Association for Professionals in Infection Control and Epidemiology. Dr. Mann is responsible for laboratory bioterrorism responsiveness within the Department of Pathology at Baylor University Medical Center. The authors have no significant financial relationships to disclose and do not address off-label or unapproved uses of any drugs.

Before beginning this activity, please read the instructions for CME on p. 333. This page also provides important information on method of physician participation, estimated time to complete the educational activity, medium used for instruction, and date of release and expiration. The quiz, evaluation form, and certification appear on pp. 333-335.

We've been told that it's just a matter of time before there is a bioterrorist attack in the USA. Although the probability that we will personally deal with bioterrorism is low, Louis Pasteur reminded us that "chance favors the prepared mind." Knowledge about bioterrorism can empower us to recognize it early and to protect ourselves when caring for these patients. We need to know about hospital plans for bioterrorism. The increased awareness can also help us with unique cases. For example, a few years ago at a local hospital, a person bleeding from the mouth and nose was brought into the emergency room. This person had just flown in from Africa, and a diagnosis of viral hemorrhagic fever had to be considered. There was a recent outbreak of Ebola in Uganda. Someone could flee that country and show up in our hospital with serious disease. We need to be prepared.

The Federal Bureau of Investigation (FBI) defines bioterrorism as "the intentional use of microorganisms or toxins de-

rived from living organisms to produce death or disease in humans, animals, or plants." This article reviews a history of biological warfare, governmental initiatives in bioterrorism, some common biological agents, epidemiologic principles, and some scenarios of bioterrorism.

HISTORY OF BIOLOGICAL WARFARE

While it is morally repugnant for us to think about using biological agents as weapons, there's a long history of it:

- In 1346, during the Siege of Kaffa, Tartars catapulted plague-infected bodies into the city. An outbreak of plague ensued.
- In 1763, during the French and Indian War, the British were said to have given blankets that had been used by smallpox patients to Native Americans.
- In World War I, a German covert operations group infected livestock in an effort to hurt the neutral trading partners of the Allies.
- From 1932 to 1945, unit 731 of the Japanese Research Program used biological weapons on prisoners of war, and the Japanese also attacked 11 Chinese cities with biological weapons. In one of those cities, there were >10,000 casualties.
- From 1942 to 1969, the USA had an offensive biological weapons program. President Nixon ordered the disbandment of this program and the destruction of the biological weapons arsenal.
- In 1972, members of the Order of the Rising Sun, a cult, were arrested for possession of *Salmonella typhae*, which they were planning to put into the water supply in midwestern cities in the USA.
- In 1979, at a military microbiological facility in Sverdlovsk, Russia, anthrax was accidentally released, causing 66 deaths.
- In 1984, the Rajneeshee cult in Oregon contaminated 10 salad bars and restaurants with *Salmonella*, resulting in an outbreak of >750 cases. (Usually the county saw ≤5 cases a

From the Departments of Epidemiology (Lathrop) and Pathology (Mann), Baylor University Medical Center, Dallas, Texas.

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Corresponding author: Linda M. Mann, PhD, Department of Pathology, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, Texas 75246 (e-mail: LindaMan@baylordallas.edu).

year.) The cult did this to influence an election. The health department considered bioterrorism as a cause of the outbreak but did not pursue it. It was not until the FBI investigated the cult for other criminal activities that it found a vial of the same strain of *Salmonella*. Members of the cult subsequently confessed and also told the FBI that they had put the agent in the city's water supply.

- In 1992, it was confirmed that Russia had extensive biological weapon programs in place.
- In 1995, it was confirmed that Iraq had anthrax and botulinum weapons and the methods for delivering them.
- In 1995, the Aum Shinrikyo released nerve gas in the Tokyo subway. The group has also attempted to disperse anthrax and botulinum toxins and to obtain Ebola virus from Zaire.

In addition, the Internet has many sites that offer recipes for biological weapons, and the number of bioterrorism hoaxes reported to the FBI has increased.

There are a number of reasons why biological agents are chosen as a means of terroristic attack. They can cause the maximum number of casualties, disrupt civil order and infrastructure, overwhelm government and emergency response systems, and create panic, confusion, and fear. The agents used tend to be highly pathogenic. A low dose can be very effective. They are highly infectious; the perpetrators themselves are protected with vaccines. Because of aerosol transmission possibilities, the agents can be weaponized. They are also easily and quickly produced, and most are environmentally stable.

Compared with other weapons of mass destruction, biological agents are easy and inexpensive to obtain. They can affect a large area, and the effects can spread quickly to outlying areas. Biological agents are hard to detect, as the agents are odorless and colorless, and the perpetrator can escape before the effects are evident. The first symptoms are nonspecific, further delaying the detection, and once bioterrorism is identified, the public may panic and medical capabilities can be overwhelmed.

Terrorists could disseminate biological agents in several ways. They could fly a plane over Texas Stadium and disperse a cloud of anthrax over the crowd, and the degree of dispersion would depend on the wind speed and turbulence. They could use vectors, such as fleas, mosquitoes, or rodents. The Japanese unit used fleas, which they dispersed through the air. They could choose bombs, artillery shells, or missiles; Iraq has that capability. They could disperse the agent through a ventilator system or add it to food and water.

GOVERNMENTAL INITIATIVES TO PREPARE FOR BIOTERRORISM

There has been considerable federal legislation on bioterrorism since the early 1990s, beginning in 1991 with the Chemical and Biological Weapons Control Act. This act gave authority to address individuals or groups who threaten or attempt to develop biological weapons and directed the Centers for Disease Control and Prevention (CDC) to establish a list of biological agents that would be potentially dangerous to the public health and to regulate the transfer and use of those agents. In 1995, the US Policy on Counterterrorism was signed, which coordinated the efforts of different federal agencies around bioterrorism and charged the FBI with crisis management. Two items of legislation were passed in 1996: the Antiterrorism and Effective Death

Penalty Act and the Defense Against Weapons of Mass Destruction Act.

The largest action taken by the federal government was passage of the Nunn-Lugar-Domenici Amendment to the Defense Authorization Act, which allocated \$100 million to enhance military response capacity, to implement assistance and training at the local and state levels, and to establish medical management strike teams. Dallas was one of the 120 cities selected to receive training. These funds provide equipment and supplies for on-scene detection, personal protection, decontamination, initial treatment, and training for first responders (i.e., firefighters, paramedics, police). However, in covert biological attacks, the first responders are not these individuals but rather health care professionals who see patients with unusual symptoms, sometimes days or weeks after the attack.

In April 2000, the CDC published *Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response*, which addresses planning, detection and surveillance, laboratory analysis, emergency response, and communications. The CDC now maintains a pharmaceutical stockpile in several locations throughout the country. It will send supplies to bioterrorism sites upon notification by the FBI and the local public health department.

On the state level, Texas received \$5.2 million in October 2000 to develop the Texas Health Alert Network (HAN). Sixty-three health departments throughout the state will receive at least \$60,000 for computer equipment, telecommunications equipment, services, and training. When the system is fully implemented, it will provide a method for quickly detecting potential danger signals such as unusual disease symptoms, abnormally large numbers of emergency room visits or 911 calls, or increases in school or workforce absences. The health department will then be able to recognize a bioterrorist event much more quickly. The Texas Disease Prevention and Control Act, chapter 81 of the Texas Health and Safety Code, already gives authority to the Texas Department of Health to quarantine infected people or to give mass immunizations.

The Association for Professionals in Infection Control and Epidemiology, Inc. (APIC) has worked with the CDC to develop the *Bioterrorism Readiness Plan: A Template for Healthcare Facilities*. The Dallas-Fort Worth APIC chapter has an active task force, which has adapted this template for use by local hospitals. These plans can be incorporated into hospitals' existing disaster plans. They identify the roles of laboratory, epidemiology, infection control, emergency, and communications personnel. The hospital communications staff will be very important in dealing with the hordes of worried people—"the worried well" who may have not been exposed at all—showing up at the hospital. The communications team will need to educate the public about the disease in question; APIC has prepared sample fact sheets that the team may wish to use.

COMMON BIOLOGICAL AGENTS

Agents that can be used in bioterrorism include bacteria (anthrax, plague, cholera, tularemia, Q fever), viruses (smallpox, Ebola/Marburg, other hemorrhagic fever or encephalitis viruses), and toxins (botulinum, staphylococcal enterotoxin B). This section will focus on 4 agents: anthrax, botulism, plague, and smallpox.

Anthrax

Anthrax is caused by *Bacillus anthracis*, a spore-forming, gram-positive bacillus. The disease can be manifested in 3 ways: pulmonary, cutaneous, and gastrointestinal. Pulmonary anthrax begins with nonspecific flulike symptoms. Two to 4 days later, there is an abrupt onset of respiratory failure and hemodynamic collapse. Shock and death generally occur within 24 to 48 hours after severe symptoms begin. Chest x-ray reveals a widened mediastinum, and gram-positive bacilli can be seen on blood culture after 2 to 3 days. Patients with cutaneous anthrax present with a papular to vesicular rash, usually on the hands, forearms, and head, and with localized itching. This form of anthrax is usually nonfatal if the patient is treated with antibiotics. Gastrointestinal anthrax causes abdominal pain, nausea, vomiting, fever, bloody diarrhea, and hematemesis. Gram-positive bacilli can be seen on blood culture. The disease is usually fatal if it progresses to toxemia and sepsis.

Because anthrax is transmitted by spores, it is usually spread by inhalation, by direct contact with the rash, or by ingestion of contaminated food. The length of the incubation period depends on the mode of transmission: for pulmonary transmission, it is 2 to 60 days; cutaneous, 1 to 7 days; and ingestion, 1 to 7 days. Anthrax is not spread person to person by the airborne route, so standard precautions prevent transmission.

An inactivated, cell-free anthrax vaccine exists, but it has limited availability and currently is given only to military personnel. Preventive measures for those who are exposed include oral fluoroquinolones, such as ciprofloxacin, levofloxacin, or ofloxacin, or doxycycline if fluoroquinolones are unavailable or contraindicated. For all cases of exposure to biological agents, health care personnel should check with the local and state health departments and the CDC for the latest recommendations.

Decontamination of patients would be necessary immediately after exposure—for instance, if a person received a letter saying, “You’ve just been exposed to anthrax.” In these cases, patients should remove their clothing, store it in a labeled plastic bag, and shower thoroughly with soap and water. The clothing will become evidence for the FBI. Because of the latency period before symptoms of anthrax appear, most patients coming in will have been exposed days before and will have already bathed and maybe even washed their clothing. If environmental surfaces need to be decontaminated, an Environmental Protection Agency–approved sporicidal/germicidal agent or a 0.5% hypochlorite solution (1 part household bleach to 9 parts water) should be used.

Patients with anthrax do not need to be given private rooms, and no special discharge instructions are needed beyond teaching home care providers the principles of standard precautions. Unfortunately, the prognosis for patients hospitalized with inhalation anthrax is poor.

Botulism

Clostridium botulinum, a gram-positive bacillus, produces a potent neurotoxin, botulinum toxin, which causes this disease. Patients with botulism are responsive and have no fever. They have symmetric cranial neuropathies (drooping eyelids, weakened jaw clench, difficulty swallowing or speaking), blurred vi-

sion, symmetric descending weakness in a proximal to distal pattern, and respiratory muscle paralysis or upper airway obstruction.

Botulism is spread by ingestion of toxin-contaminated food, but aerosolization of the toxin would probably be the mechanism chosen for bioterrorism. The incubation period for foodborne exposure is 12 to 36 hours; for inhalation exposure, 24 to 72 hours. Botulism is not transmitted person to person. Thus, by following standard precautions, spread of the disease can be prevented. That is an important point to stress to hospital staff and the public.

The Department of Defense has developed a botulism vaccine, which is available as an investigational new drug. A trivalent botulism antitoxin is available from the state health department or the CDC for use after exposure. If the antitoxin is used, the patient should be skin tested for hypersensitivity before administration.

Plague

Plague, an acute bacterial disease resulting in lymphatic (bubonic plague) or pulmonary (pneumonic plague) infections as well as septicemia, is caused by *Yersinia pestis*, a gram-negative bacillus. Clinical features of plague include fever, cough, chest pain, hemoptysis, and a mucopurulent or watery sputum containing gram-negative rods. X-ray findings would be consistent with pneumonia. Besides being spread through dispersion of aerosol, as would be expected in bioterrorism, pneumonic plague can be spread from an infected rodent to a person by means of infected fleas and person to person through large droplet aerosol. The incubation period is 2 to 8 days for fleaborne transmission and 1 to 3 days for pulmonary exposure. The period of communicability lasts until a patient has completed 72 hours of antimicrobial therapy.

Early administration of antibiotics is key to treatment. Currently, no plague vaccine is available in the USA. After exposure, doxycycline and ciprofloxacin are recommended for prophylaxis. The need for decontamination is the same as with anthrax: it is useful only immediately after exposure.

For infection control, the patient should be placed in a private room (or in a room with other plague patients) and put on droplet precautions, in addition to standard precautions. The physician and staff should limit the patient’s movement to essential medical purposes only; if a patient must leave the room, he or she should wear a surgical-type mask.

Smallpox

In 1980, the World Health Organization declared that smallpox was globally eradicated. Also at this time, routine vaccinations for children and the military were discontinued in the USA. A large percentage of the population, then, would be susceptible to smallpox. Even people who were vaccinated as children would not be protected. It was believed that only 2 places in the world still had live cultures of the smallpox virus (*Variola major*): the CDC and a facility in Russia. Unfortunately, the Russian facility was not completely secure, and the virus may be in the hands of terrorists.

With smallpox, the patient develops a 2- to 4-day nonspecific prodrome of fever, myalgias, and rash. The rash has a synchro-

nous onset and is most prominent on the face and extremities, including the palms and soles. The rash scabs over in 1 to 2 weeks.

Smallpox is transmitted patient to patient from airborne droplet exposure and by contact with skin lesions or secretions. The incubation period is 7 to 17 days, with an average of 12 days. Patients are most infectious just prior to development of the rash and remain infectious until the scabs separate—a period of about 3 weeks.

The live-virus intradermal vaccine that's available is effective if given within 3 days of exposure. Currently, the vaccine is not available in sufficient quantity to vaccinate the entire populace. A company has just been awarded a contract to start producing smallpox vaccine, but it will take years before the product will be available.

Airborne and contact precautions are required when caring for smallpox patients. Such transmission-based precautions have been shown to work—the CDC has been able to halt Ebola outbreaks using transmission-based precautions. Patients should be placed in a private room with 6 to 12 air exchanges, negative air pressure, and an anteroom; the door should be closed at all times. If there were an outbreak of smallpox, hospital facilities would be quickly overwhelmed, and these patients would need to be cared for at home, with their caregivers using precautions. Bringing the patients into the hospital would expose many people to the disease. Medical and nursing staff must wear personal protective equipment with respirator masks of N95 or higher. Transport of the patient should be limited to essential medical needs, and if the patient were to leave the room, he or she would need to wear a surgical-type mask.

Patient decontamination after exposure is not indicated. Individuals who are exposed to the virus should not only receive the vaccine but also monitor themselves for flulike symptoms or rash during the incubation period to minimize the risk of exposure to others.

EPIDEMIOLOGIC PRINCIPLES

The first step in preparing for bioterrorism is to maintain a high level of suspicion in a number of clinical situations:

- A rapidly increasing disease incidence (e.g., within hours or days) in a normally healthy population
- An epidemic curve that rises and falls during a short period of time
- An unusual increase in the number of people seeking care, especially with fever, respiratory, or gastrointestinal complaints
- An endemic disease rapidly emerging at an uncharacteristic time or in an unusual pattern (e.g., diseases usually spread by fleas in people who have no evidence of flea bites or no recent history of being near animals)
- Lower attack rates among people who have been indoors, especially in areas with filtered air or closed ventilation systems, compared with people who have been outdoors
- Clusters of patients arriving from a single locale
- Large numbers of rapidly fatal cases
- Any patient presenting with a disease that is relatively uncommon and has bioterroristic potential (e.g., pulmonary anthrax, plague, smallpox)
- Concurrent reports of increased animal deaths

The second step is to develop and use epidemiologic tools, including routine surveillance and disease-reporting mechanisms. Baylor's epidemiologists contact the health department routinely to report diseases, and occasionally the health department contacts them to see if they've seen certain conditions. The epidemiology department and the hospital laboratory already work together to identify outbreaks. For example, if laboratory personnel identify 2 or more patients with an unusual organism, they notify the epidemiology department, which determines if there is a correlation between the patients. Pertinent information would be relayed to the local health department as needed. Communication is key—involving hospitals, the public health system, the emergency medical system, police and FBI, medical examiners, and veterinarians.

Local response plans are needed. Hospitals need to determine whether they would have enough ventilators and, if they don't, what they would do while they were waiting for the CDC to send supplies. Other elements of a local response plan include identifying the agent, having vaccines and treatment drugs available, reinforcing standard and transmission-based precautions, planning a script for communicating with the public, developing training for medical personnel, performing early reporting, and conducting drills to identify any weaknesses in the plan.

SCENARIOS OF BIOTERRORISM

The following sections describe the laboratory response to potential scenarios for bioterrorism.

The hoax

The most common scenario for bioterrorism is the hoax: for example, a letter with powder in it that says, "You've just been exposed to anthrax." In this situation, the person opening the letter should not panic. He or she should leave the room and call 911. The 911 operators will connect the person with the North Texas Joint Terrorism Task Force of the FBI, which will investigate. The task force will ensure that appropriate measures are taken for safety and for the legal prosecution of the perpetrators.

The massive attack

In a massive attack, most likely a chemical or biotoxin attack, people will be collapsing in the streets, and the FBI and CDC will soon be present to manage the situation. Once the agent is identified, health care workers will provide treatment that is empiric and supportive. Many health care workers will be affected by the attack themselves. During a massive outbreak, local laboratories will bear little responsibility for identification of the agent or management of individual patients.

The small or covert attack

This is the situation most to be feared and planned for: a few sick people showing up in doctors' offices and emergency departments. Many will be told to go home, rest, and drink liquids. As some of them get sicker, specimens will be sent for culture, and hospital laboratories will have an opportunity to help identify bioterroristic agents. Because most hospital laboratories are not set up to deal with these agents, their job is to recognize the possibility of having such an agent and to quickly refer it to a laboratory that can make the definitive diagnosis.

Baylor University Medical Center, like most hospitals, has a level A clinical laboratory, which has been asked by the CDC to rule out *Bacillus anthracis*, *Brucella* species, *Francisella tularensis*, and *Yersinia pestis* as part of the bioterrorism preparedness. In situations like this, the clinical laboratory will refer the specimen to higher-level laboratories. The county laboratory is a level B laboratory. It is set up to do fluorescent antibody stains on isolates within a few hours. The state laboratory in Austin is a level C laboratory. It can test for botulism toxin and can use electron microscopy to identify viruses such as smallpox and Ebola. Soon it will have real-time polymerase chain reaction testing as well. CDC and the US Army Medical Research Institute of Infectious Diseases are both level D laboratories, with P4 maximum containment facilities and the ability to handle whatever comes their way.

CONCLUSION

The threat of bioterrorism is real. To prepare for it, we must educate our health care team, incorporate bioterrorism preparedness into disaster plans, and support cooperation and communication between the public health department and hospitals.

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